Commentary

Noninvasive ventilation for acute lung injury: how often should we try, how often should we fail?

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See related research article by Rana *et al*., http://ccforum.com/content/10/3/R79

Abstract

The selection of patients with acute lung injury/acute respiratory distress syndrome (ALI/ARDS) to receive noninvasive ventilation (NIV) is challenging, partly because there are few reliable selection criteria. The study by Rana and colleagues in the previous issue of *Critical Care* identifies metabolic acidosis and a lower oxygenation index as predictors of NIV failure, although it is unable to identify threshold values. It also demonstrates that treating patients with NIV for ALI/ARDS and shock is an exercise in futility. Future studies need to focus on criteria that will enable selection of patients for whom NIV will have a high likelihood of success.

Although noninvasive ventilation (NIV) has been used to treat acute respiratory failure for well over a decade, our knowledge on how best to apply it continues to evolve. Relatively little debate surrounds its use for acute respiratory failure due to exacerbations of chronic obstructive pulmonary disease [1], cardiogenic pulmonary edema [2] or in immunocompromised hosts [3]. However, its appropriate use to treat hypoxemic respiratory failure, particularly patients with acute lung injury/acute respiratory distress syndrome (ALI/ARDS), remains unclear. In the previous issue of *Critical Care*, Rana and colleagues [4] examine this application of NIV and identify risk factors for failure.

Rana and colleagues [4] evaluated the outcomes of an observational cohort of patients with ALI treated with NIV as the initial mode of therapy. Of a total of 358 patients started on NIV at one hospital over a 6 month period, 79 were identified as having ALI as defined by bilateral chest infiltrates, a PaO_2/FiO_2 <300 and no evidence of left heart failure. After excluding do not recussitate/do not intubate patients and two who declined to participate, 54 patients were left for analysis. Two-thirds of this group (38 patients or 70.3%) failed NIV, including all 19 patients with shock. When those patients without shock were evaluated in a multivariate logistic regression analysis, metabolic acidosis (odds ratio 1.27, 95% confidence interval 1.03-0.07 per unit of base deficit) and severe hypoxemia (odds ratio 1.03, 95% confidence interval 1.01-1.05 per unit decrease in PaO_2/FiO_2) remained significant predictors of NIV failure. Although statistically significant, these odds ratios demonstrate a very weak association.

Identifying factors that reliably predict NIV failure is desirable so that patients likely to fail can be excluded. Antonelli and colleagues [5] found that a PaO_2/FiO_2 ratio of 146 or less after one hour of NIV was an independent risk factor for intubation (odds ratio 2.51). The Rana study found that the mean PaO_2/FiO_2 in the NIV success group was 147 and 112 in the failure group, but the timing of the measurement relative to the initiation of NIV was not specified. Also, although patients who showed improved oxygenation with NIV tended to have better outcomes, this did not reach significance. The small numbers and lack of a clear oxygenation threshold for NIV failure limits the clinical applicability of these data. Acidosis has also been identified as a predictor of NIV failure in earlier trials [6], and the finding by Rana and colleagues that metabolic acidosis was associated with NIV failure, reflected the greater severity of illness in the patients who failed. Again, the lack of a threshold value for acidosis limits the clinical applicability of these findings. Nonetheless, the findings underline the importance of obtaining baseline arterial blood gases when assessing ALI/ARDS patients for receipt of NIV.

Considering that hypotensive shock has been considered a contraindication to NIV in many of the controlled trials [7], it is a bit shocking that 35% of the patients who were included in the Rana cohort had septic shock. Although the authors are

ALI/ARDS = acute lung injury/acute respiratory distress syndrome; NIV = noninvasive ventilation.

correct in stating that no prior evidence supported the proscription, their finding that all 19 patients with septic shock who were placed on NIV failed should lay the issue to rest and solidify the place of septic shock on the list of contraindications to NIV. Limitations of cohort analyses like that of Rana and colleagues include the lack of prospective criteria for initiation of NIV and intubation in the face of NIV failure. Thus, findings might reflect the biases of clinicians managing the patients. Patients with worse oxygenation indexes or metabolic acidoses or septic shock are intubated because the clinicians were responding to preconceived biases and the predictors, in essence, are self-fulfilling prophecies. Lacking a control group, this possibility cannot be rejected. The lack of controls also precludes any conclusions about efficacy. This is a particular limitation when interpreting the finding that outcomes were much better in patients succeeding on NIV than in those who failed (mortality none versus 68%, respectively). This finding is predictable, of course – those who avoid intubation tend to do well. But lacking controls, it is impossible to know whether the group as a whole (successes and failures) did better – or worse – than it would have had intubation been the initial therapy. This is of particular concern in view of the trial of Esteban and colleagues [8], which showed an increased intensive care unit mortality among NIV patients whose intubation was delayed compared to controls. The concern is that some patients treated with NIV as initial therapy might have had their needed intubations delayed. In addition to conferring better outcomes on the successes, NIV might have worsened outcomes in patients whose intubations were delayed. The study by Squadrone and colleagues [9] is reassuring in this regard in that it demonstrated that patients failing NIV fared no worse than patients intubated from the start, but the patients had chronic obstructive pulmonary disease, not ALI/ARDS.

An interesting and provocative speculation by the authors is that the higher tidal volumes among patients who failed NIV contributed to excessive lung stretch, worsening lung injury and contributing to NIV failure. It seems at least equally likely that the larger tidal volumes were markers of more severe disease, reflecting higher rates of catabolism and larger dead spaces, and this explains the worse outcomes. However, we agree that it is an intriguing hypothesis that requires more study.

What messages should we take away from the study by Rana and colleagues regarding the selection of appropriate ALI patients for a trial of NIV? Is there a severity of acute respiratory failure beyond which NIV should not be used? With our current NIV technology, it seems sensible to exclude patients from consideration who have multi-organ dysfunction, or are poor candidates for NIV by virtue of inability to cooperate or protect the airway, or because of excessive secretions. Clearly, NIV should be avoided in patients with shock, severe hypoxemia or acidosis. The more difficult issue is whether there is a threshold of severity for hypoxemia and acidosis beyond which NIV should be considered contraindicated. Unfortunately, the answer remains; we still don't know. The study by Rana and colleagues does not provide sufficient precision to answer the question, even in the context of prior studies. For now, we recommend selecting ALI/ARDS patients for NIV according to general selection guidelines [10]. These patients should be closely monitored in an intensive care unit setting and, if there is no improvement in oxygenation (PaO_2/FiO_2 into the range of 150), pH or vital signs within the first 1 to 2 hours, intubated. The greatest value of the Rana and colleagues study is to highlight the need for larger prospective studies to better define criteria for selecting ALI/ARDS patients for NIV.

Competing interests

The authors declare that they have no competing interests.

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